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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	10

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/086,169	Applicant(s) RABINDRAN ET AL.	
	Examiner Shaojia A Jiang	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-28 and 57-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-28 and 57-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on January 14, 2004 wherein claims 13-28 and 57-59 have been amended and claims 34-38, 61, and 63 are cancelled. As recorded in the previous Office Action July 15, 2003, claims 1-12, 29-33, 39-56, 60 and 62 have been cancelled previously.

Currently, claims 13-28 and 57-59 are pending in this application.

Claims 13-28 and 57-59 as amended now are examined on the merits herein.

Applicant's amendment amending claims 13-14, 17-19, 21, 23-25 and 28 and Applicant's remarks, filed January 14, 2004 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of scope of enablement of record stated in the Office Action dated July 15, 2003 have been fully considered and are found persuasive to overcome the rejection. Therefore, the said rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 57-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the same reasons of record stated in the Office Action dated July 15, 2003.

Applicant's remarks filed January 14, 2004 with respect to this rejection under 35 U.S.C. 112, second paragraph in the previous Office Action have been fully considered but are not deemed persuasive to remove the rejection.

Applicant asserts that R7 and R8 are fully described in claims 57-59.The examiner notes the recitations "**R7** NH(CH2)v or ..." and "**R7** is H or ...", and "**R8** is selected from ..." in claims 57-59. However, it is unclear as to how and where R7 and R8 are related to the Formula (I) since there are **no** R7 and R8 in the formula I. Therefore, the scope of claims is indefinite as to the compound having the Formula (I) employed in the claimed method encompassed thereby.

The following is new rejections necessitated by Applicant's amendment filed on January 14, 2004.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13, 15, 17-18, 20, 23-24, 26 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Abe et al. (Br. J. Cancer, 1995, 72, page 418-423, of record).

Abe et al. discloses the method of determining the chemosensitization of spontaneous multidrug resistance (i.e., the overexpression of MRP/p-gp or MDR1 and non-P-gp-mediated multidrug resistance) in human cancer cells exhibiting such

resistance comprising the instant method steps and also administering an effective amount of a chemosensitizing reversal agent such as verapamil in combination with a chemotherapeutic agent such as doxorubicin, concurrently with or after administration. See Abe et al., the entire article particularly Summary and both the left and right coloum at page 418; the method steps or the procedure and results at page 419-421. The method of Abe et al. inherently distinguish P-gp/MRP multiple drug resistance from BCRP or other non-P-gp/non MRP multiple drug resistance, and determine the presence and magnitude of cancer cell BCRP or other non-P-gp/non MRP multiple drug resistance in cancer cells exhibiting such resistance since Abe's method steps are same as the instant method steps. See *Ex parte Novitski*, 26 USPQ 2d 1389. Thus, the administration of the same active agents inherently treat the same cancer cells under the doctrine of inherency. See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it related to the claimed invention herein. Thus, Abe et al. anticipates claims 13, 15, 17-18, 20, 23-24, 26 and 28.

Claims 13-15, 17-20, 23-26 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Tasaki et al. (J. Urology 1995, 154, page 1210-1216, of record).

Tasaki et al. teaches that the methods of reversal the non-P-gp-mediated multidrug resistance in human prostatic cancer cells exhibiting such resistance comprising the instant method steps and administering an effective amount of a chemosensitizing reversal agent such as a 1,4-dihydropyridine derivative (NIK250), in

combination with a chemotherapeutic agent such as etoposide, doxorubicin and mitoxantrone (see Table 2 at page 1212), prior to, concurrently with or after administration are known in the art. See also Tasaki et al., the entire article particularly abstract; the right column of page 1210, the method steps or the procedure and results at page 1210-1214. Tasaki et al. also teaches the method therein increases in cancer cell death by about 22% above or about 13% above (see Figure 3 at the right column of page 1213). The method of Tasaki et al. inherently distinguish P-gp/MRP multiple drug resistance from BCRP or other non-P-gp/non MRP multiple drug resistance, and determine the presence and magnitude of cancer cell BCRP or other non-P-gp/non MRP multiple drug resistance in cancer cells exhibiting such resistance since Tasaki's method steps are same as the instant method steps. See *Ex parte Novitski*, 26 USPQ 2d 1389. Thus, the administration of the same active agents inherently treat the same cancer cells under the doctrine of inherency. See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it related to the claimed invention herein. Thus, Tasaki et al. anticipates claims 13-15, 17-20, 23-26 and 28.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16, 21, 27, and 57-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasaki et al. (J. Urology 1995, 154, page 1210-1216, of record) and Cui et al. (of record).

The same disclosure of Tasaki et al. has been discussed in the 102(b) rejection set forth above.

The prior art does not expressly disclose the employment of the particular chemosensitizing reversal agent fumitremorgin C in combination with the particular chemotherapeutic agent such as doxorubicin and mitoxantrone in methods of distinguishing P-gp/MRP multiple drug resistance from BCRP or other non-P-gp/non MRP multiple drug resistance, and a method of determining the presence and magnitude of cancer cell BCRP or other non-P-gp/non MRP multiple drug resistance in cancer cells exhibiting such resistance.

Cui et al. discloses that the particular agents, fumitremorgin C (known to be covered and encompassed by the Formula (I) herein, CAS Registry number: 118974-02-0 and its structure, PTO-892) or diketo piperazine derivatives from Aspergillus are neoplasm inhibitors, and are hence useful in the treatment of tumor and/or cancer. See abstract.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ of the particular chemotherapeutic agent such as doxorubicin and mitoxantrone in combination with the particular chemosensitizing reversal agent such as fumitremorgin C in methods of distinguishing P-gp/MRP multiple drug resistance from BCRP or other non-P-gp/non MRP multiple drug resistance, and a

method of determining the presence and magnitude of cancer cell BCRP or other non-P-gp/non MRP multiple drug resistance in cancer cells exhibiting such resistance.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ of the particular chemotherapeutic agent such as doxorubicin and mitoxantrone in combination with the particular chemosensitizing reversal agent such as fumitremorgin C in methods of distinguishing P-gp/MRP multiple drug resistance from BCRP or other non-P-gp/non MRP multiple drug resistance, and a method of determining the presence and magnitude of cancer cell BCRP or other non-P-gp/non MRP multiple drug resistance in cancer cells exhibiting such resistance since doxorubicin or mitoxantrone, and fumitremorgin C or diketo piperazine derivatives from Aspergillus, are known to be useful in a method of treating particular cancer based on the prior art. Therefore, one of ordinary skill in the art would have reasonably expected that combining doxorubicin or mitoxantrone, and fumitremorgin C or diketo piperazine derivatives from Aspergillus known useful for the same purpose in a composition to be administered would improve the therapeutic effect for treating particular cancer.

Since all active composition components herein are known to useful to treat particular cancers, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's arguments filed January 14, 2004 with respect to the prior art rejections in the previous Office Action have been considered but are moot in view of the new ground(s) of rejection above.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
May 13, 2004

SHAOJIA ANNA JIANG
PATENT EXAMINER